

in the art as interconnections or leads). The insulating substrate is generally, but not always, a polymer. As is known in the art, one or a plurality of layers may be used, to make either "two dimensional" (e.g. all electrodes and interconnections in a plane) or "three dimensional" (wherein the electrodes are on one surface and the interconnects may go through the board to the other side) boards. Three dimensional systems frequently rely on the use of drilling or etching, followed by electroplating with a metal such as copper, such that the "through board" interconnections are made. Circuit board materials are often provided with a foil already attached to the substrate, such as a copper foil, with additional copper added as needed (for example for interconnections), for example by electroplating. The copper surface may then need to be roughened, for example through etching, to allow attachment of the adhesion layer.

[0248] Accordingly, in a preferred embodiment, the present invention provides biochips (sometimes referred to herein "chips") that comprise substrates comprising a plurality of electrodes, preferably gold electrodes. The number of electrodes is as outlined for arrays. In "electron transfer mode", preferably each electrode preferably comprises a self-assembled monolayer as outlined herein. In a preferred embodiment, one of the monolayer-forming species comprises a capture ligand as outlined herein. In addition, each electrode has an interconnection, that is attached to the electrode at one end and is ultimately attached to a device that can control the electrode. That is, each electrode is independently addressable.

[0249] The substrates can be part of a larger device comprising a detection chamber that exposes a given volume of sample to the detection electrode. Generally, the detection chamber ranges from about 1 nL to 1 mL, with about 10 μ L to 500 μ L being preferred. As will be appreciated by those in the art, depending on the experimental conditions and assay, smaller or larger volumes may be used.

[0250] In some embodiments, the detection chamber and electrode are part of a cartridge that can be placed into a device comprising electronic components (an AC/DC voltage source, an ammeter, a processor, a read-out display, temperature controller, light source, etc.). In this embodiment, the interconnections from each electrode are positioned such that upon insertion of the cartridge into the device, connections between the electrodes and the electronic components are established.

[0251] Detection electrodes on circuit board material (or other substrates) are generally prepared in a wide variety of ways and are described in the references outlined above.

[0252] The electrodes described herein are depicted as a flat surface, which is only one of the possible conformations of the electrode and is for schematic purposes only. The conformation of the electrode will vary with the detection method used. For example, flat planar electrodes may be preferred for optical detection methods, or when arrays of nucleic acids are made, thus requiring addressable locations for both synthesis and detection. Alternatively, for single probe analysis, the electrode may be in the form of a tube, with the SAMs comprising conductive oligomers and nucleic acids bound to the inner surface. Electrode coils may be preferred in some embodiments as well. This allows a maximum of surface area containing the nucleic acids to be exposed to a small volume of sample.

[0253] In "impedance mode" the detection electrode can comprise a coating of conductive polymers or oligomers. By "conductive oligomer" herein is meant a substantially conducting oligomer, preferably linear, some embodiments of which are referred to in the literature as "molecular wires". By "substantially conducting" herein is meant that the oligomer is capable of transferring electrons at 100 Hz. Generally, the conductive oligomer has substantially overlapping n-orbitals, i.e. conjugated n-orbitals, as between the monomeric units of the conductive oligomer, although the conductive oligomer may also contain one or more sigma (σ) bonds. Additionally, a conductive oligomer may be defined functionally by its ability to inject or receive electrons into or from an associated ETM. Furthermore, the conductive oligomer is more conductive than the insulators as defined herein. Additionally, the conductive oligomers of the invention are to be distinguished from electroactive polymers, that themselves may donate or accept electrons.

[0254] In a preferred embodiment, the conductive oligomers have a conductivity, S, of from between about 10^{-5} to about $10^4 \Omega^{-1} \text{ cm}^{-1}$, with from about 10^{-5} to about $10^3 \Omega^{-1}$ being preferred, with these S values being calculated for molecules ranging from about 20 Å to about 200 Å. As described below, insulators have a conductivity S of about $10^{-7} \Omega^{-1} \text{ cm}^{-1}$ or lower, with less than about $10^{-8} \Omega^{-1} \text{ cm}^{-1}$ being preferred. See generally Gardner et al., *Sensors and Actuators A* 51 (1995) 57-66, incorporated herein by reference.

[0255] Desired characteristics of a conductive oligomer include high conductivity, sufficient solubility in organic solvents and/or water for synthesis and use of the compositions of the invention, and preferably chemical resistance to reactions that occur i) during binding ligand synthesis (i.e. nucleic acid synthesis, such that nucleosides containing the conductive oligomers may be added to a nucleic acid synthesizer during the synthesis of the compositions of the invention, ii) during the attachment of the conductive oligomer to an electrode, or iii) during binding assays. In addition, conductive oligomers that will promote the formation of self-assembled monolayers are preferred.

[0256] The oligomers of the invention comprise at least two monomeric subunits, and can include homo- and hetero-oligomers, and include polymers. Generally, oligomers of the invention comprise charge neutral conjugated polymers, see generally U.S. Ser. No. 09/962,913, hereby incorporated by reference. Suitable conductive polymers include, but are not limited to, polypyrrole, polythiophene, polyaniline, polyfuran, polypyridine, polycarbazole, polyphenylene, poly(phenylenevinylene), polyfluorene, polyindole, derivatives thereof, co-polymers thereof, and combinations thereof. Preferably the conductive polymer is polypyrrole, polythiophene and polyaniline, and most preferable is polypyrrole. See generally U.S. Ser. No. 60/314,611, hereby incorporated by reference.

[0257] In "electron transfer mode", the detection electrode comprises a self-assembled monolayer (SAM) comprising conductive oligomers. By "monolayer" or "self-assembled monolayer" or "SAM" herein is meant a relatively ordered assembly of molecules spontaneously chemisorbed on a surface, in which the molecules are oriented approximately parallel to each other and roughly perpendicular to the surface. Each of the molecules includes a functional group